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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,292	01/30/2002	James L. Hartley	0942.285000H/RWE/BJD	3058

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,292	HARTLEY ET AL.-20040920	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-227* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *151-157 and 213-225* is/are allowed.

6)☒ Claim(s) *35-150,158-212,226 and 227* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response, filed 6/23/2004, in which several claims were amended (claims 35, 57, 78, 96-97, 115, 132-133, 149, 151, 159, 187, 196-197, 213) and in which new claims were added (claims 226-227). Claims 35-227 are pending and under consideration in the instant application.

Any rejection of record not addressed herein is withdrawn. This action is FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-58, 96-97, 132-133 and 196-197 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 6/23/2004.**

Each of the amended claims recites "immediately adjacent to". There is no literal support in the originally filed specification or claims for the cited phrase. Therefore, the term is impermissible NEW MATTER.

Claims 35-150, 159-212 & 226-227 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 6/23/2004.**

Each of the rejected claims has been amended to recite, "wherein said at least one recombination protein is not a transposase". There is no literal support anywhere in the specification as originally filed for the cited phrase. Therefore, the newly added negative limitation is impermissible NEW MATTER.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35-71, 74-77, 158-180 and 183-186 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (WO 93/19172, of record; see the entire application). **This rejection is maintained for reasons of record in the previous office action mailed 3/23/2004 and which are repeated below.**

Johnson et al teach methods for producing members of specific binding pairs featuring the use of recombinant bacteriophage to display functional antibodies (e.g. scFv; see, for

example, pages 19, 26-34, 46-47, 49 and 52). Their methods include a method of producing a nucleic acid molecule by providing a first nucleic acid molecule comprising a first portion of a gene and a recombination site, a second nucleic acid molecule comprising a second protein of a gene and a recombination site, mixing *in vitro* or *in vivo* the first and second nucleic acids with a recombination protein to recombine the first and second nucleic acids to form a third nucleic acid, thereby forming an operably linked and functional gene from the first and second portions of the gene. Johnson et al teach the recombination of immunoglobulin genes in a phage that expressed the recombined immunoglobulin genes by joining the recombined immunoglobulin with a promoter that causes the expression of the recombined immunoglobulin genes on the surface of the phage (e.g. pages 26-34). The gene may encode a selectable marker or a heterodimeric product (e.g. pages 32 and 47). The first or second portion of the gene may be fragments of the gene and may comprise a promoter and may further be a PCR product (e.g. pages 32 and 52). The first and second portions of the gene may be located adjacent to the recombination site, and the first or second nucleic acid molecule may comprise a cloning site (e.g. pages 19, 26-27, 31-32 and 46). The first, second or third nucleic acid may be an expression vector and may be linear. The functional gene may be expressed in a host cell and may be selected (e.g. phage display). The host cell may be *E. coli* (e.g. pages 26-34). The recombination sites may be loxP sites or att sites. The recombination protein may be Cre, Int, IHF, Xis, Flp, gamma-delta, Tn3, Hin, Gin or Cin (e.g. pages 26-34). Johnson et al teach that additional recombination sites may be present on the recombination substrates (e.g. pages 22-23). Johnson et al teach that the vector FdDOG-1 is derived from pUC19, which has multiple cloning sites.

Response to Arguments

Applicant's arguments filed 6/23/2004 have been fully considered but they are not persuasive. The response filed 6/23/2004 essentially argues that the amendment of some of the claims to recite the limitation that the functional gene that is formed by the recombination of the first and second nucleic acids is an antibiotic resistance gene obviates the rejection of those claims. Arguments presented previously in response to similar grounds of rejection using the same reference are incorporated by reference into the 6/23/2004 response. The response further argues that Johnson et al is not enabling for *in vitro* recombination reactions featuring the Cre recombinase and LoxP sites.

To the extent that arguments made previously and incorporated by reference in the latest response are still applicable to the rejected claims, the examiner's arguments to rebut the previous arguments are incorporated herein by reference as well. Applicants' amendment to some of the claims to recite that the promoter and its antibiotic resistance gene or portion thereof are operably linked "to form a functional antibiotic resistance gene" has obviated the grounds of rejection over Johnson et al, and the rejection has been withdrawn for those claims.

The argument that the Johnson et al reference is not enabling for embodiments featuring the Cre recombinase and LoxP sites misses at least two points: (i) the invention taught by Johnson et al is not limited to embodiments that feature the Cre recombinase, and (ii) the response ignores the teachings of Boyd et al (Nucleic Acids Research, Vol. 21, pages 817-821, 1993), which teach that the Cre recombinase efficiently catalyzes recombination *in vitro*. The response cites a passage at page 6, lines 1-16 of the specification as indicating that it was unpredictable at the time of filing to practice *in vitro* recombination between different vectors for

several reasons (e.g. site specificities and efficiencies were expected to differ *in vitro*, the topology of the DNA substrates and recombination proteins were expected to differ significantly *in vitro* versus *in vivo*, reaction times were expected to be longer than the stability of the recombination enzymes *in vitro*). The cited passage indicates that *in vitro* recombination reactions were not expected to be sufficiently efficient to yield the desired levels of products. The response does not clearly indicate, for example, whether any of the barriers were overcome by their own experimental procedures or other intervening art. While it may have been true at the time of the Johnson et al application that it would have required some experimentation to optimize recombination reaction conditions, such experimentation would have been routine, as indicated by both the Johnson et al and Boyd et al references (e.g. Boyd et al teach that Cre-mediated recombination *in vitro* is efficient and Johnson teach a methodology that can be readily used to determine whether the desired recombination products are formed).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-58, 96-97, 132-133 and 196-197 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Each of the claims recite the limitation that the first or second gene, or portion thereof, is located "immediately adjacent" to a given recombination site (e.g. claims 57-58, 96-97, 132-133, 196-197). The term "immediately adjacent" is not defined in the specification and it is unclear

the structural/functional requirements for satisfying this limitation. Does the term necessarily mean that the recombination site is "immediately adjacent" to the gene or portion thereof with no intervening nucleotides? Or can some unspecified number of nucleotides be present between the portion of the gene and the recombination site and still meet the limitation of being "immediately adjacent"? While it is understood that in making a similar rejection in the previous office action the examiner presented the phrase "immediately adjacent" to mean that there are no nucleotides between the different elements, this does not mean that the term is necessarily limited to this interpretation by the instant specification (e.g. see the New Matter rejection above) or prior art. The term "immediately adjacent" is not clearly defined in the prior art and is subjective.

Conclusion

Claims 35-227 are pending in the instant application, with claims 151-157 & 213-225 are allowable. Claims 35-150, 158-212 & 226-227 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

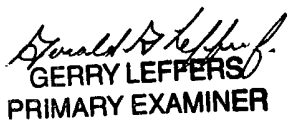
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

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